inclusion body myopathy with early-onset Paget disease and frontotemporal dementia

Inclusion body myopathy with early-onset Paget disease and frontotemporal dementia (IBMPFD) is a condition that can affect the muscles, bones, and brain.

The first symptom of IBMPFD is often muscle weakness (myopathy), which typically appears in mid-adulthood. Weakness first occurs in muscles of the hips and shoulders, making it difficult to climb stairs and raise the arms above the shoulders. As the disorder progresses, weakness develops in other muscles in the arms and legs. Muscle weakness can also affect respiratory and heart (cardiac) muscles, leading to life-threatening breathing difficulties and heart failure.

About half of all adults with IBMPFD develop a disorder called Paget disease of bone. This disorder most often affects bones of the hips, spine, and skull, and the long bones of the arms and legs. Bone pain, particularly in the hips and spine, is usually the major symptom of Paget disease. Rarely, this condition can weaken bones so much that they break (fracture).

In about one-third of people with IBMPFD, the disorder also affects the brain. IBMPFD is associated with a brain condition called frontotemporal dementia, which becomes noticeable in a person's forties or fifties. Frontotemporal dementia progressively damages parts of the brain that control reasoning, personality, social skills, speech, and language. People with this condition initially may have trouble speaking, remembering words and names (dysnomia), and using numbers (dyscalculia). Personality changes, a loss of judgment, and inappropriate social behavior are also hallmarks of the disease. As the dementia worsens, affected people ultimately become unable to speak, read, or care for themselves.

People with IBMPFD usually live into their fifties or sixties.

Frequency

Although the prevalence of IBMPFD is unknown, this condition is rare. It has been identified in about 26 families.

Genetic Changes

Mutations in the *VCP* gene cause IBMPFD. The *VCP* gene provides instructions for making an enzyme called valosin-containing protein, which has a wide variety of functions within cells. One of its most critical jobs is to help break down (degrade) proteins that are abnormal or no longer needed.

Mutations in the *VCP* gene alter the structure of valosin-containing protein, disrupting its ability to break down other proteins. As a result, excess and abnormal proteins may build up in muscle, bone, and brain cells. The proteins form clumps that interfere with the normal functions of these cells. It remains unclear how damage to muscle, bone, and brain cells leads to the specific features of IBMPFD.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

In some cases, an affected person inherits the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- IBMPFD
- Inclusion body myopathy with early-onset Paget disease of bone and/or frontotemporal dementia
- Inclusion body myopathy with Paget disease of bone and/or frontotemporal dementia
- Lower motor neuron degeneration with Paget-like bone disease
- Muscular dystrophy, limb-girdle, with Paget disease of bone
- Pagetoid amyotrophic lateral sclerosis
- Pagetoid neuroskeletal syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Inclusion body myopathy with early-onset paget disease and frontotemporal dementia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1833662/

Other Diagnosis and Management Resources

- GeneReview: Inclusion Body Myopathy with Paget Disease of Bone and/or Frontotemporal Dementia
  https://www.ncbi.nlm.nih.gov/books/NBK1476

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Dementia
  https://medlineplus.gov/dementia.html
- Health Topic: Muscle Disorders
  https://medlineplus.gov/muscledisorders.html
- Health Topic: Paget's Disease of Bone
  https://medlineplus.gov/pagetsdiseaseofbone.html

Genetic and Rare Diseases Information Center

- Inclusion body myopathy with early-onset Paget disease and frontotemporal dementia
  https://rarediseases.info.nih.gov/diseases/10899/inclusion-body-myopathy-with-early-onset-paget-disease-and-frontotemporal-dementia

Additional NIH Resources

- National Institute of Arthritis and Musculoskeletal and Skin Diseases: Paget's Disease of Bone
  https://www.niams.nih.gov/Health_Info/Bone/Pagets/
- National Institute of Neurological Disorders and Stroke: Frontotemporal Dementia Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Frontotemporal-Dementia-Information-Page
- National Institute of Neurological Disorders and Stroke: Myopathy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Myopathy-Information-Page

Educational Resources

- Disease InfoSearch: Inclusion body myopathy with early-onset paget disease and frontotemporal dementia
  http://www.diseaseinfosearch.org/Inclusion+body+myopathy+with+early-onset+paget+disease+and+frontotemporal+dementia/8654
- MalaCards: inclusion body myopathy with early-onset paget disease and frontotemporal dementia
  http://www.malacards.org/card/inclusion_body_myopathy_with_early_onset_paget_disease_and_frontotemporal_dementia
- Neuromuscular Disease Center, Washington University
  http://neuromuscular.wustl.edu/musdist/distal.html#dmdpaget
- Orphanet: Inclusion body myopathy with Paget disease of bone and frontotemporal dementia
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=52430
- University of California, San Francisco (UCSF) Memory and Aging Center: Frontotemporal Dementia
  http://memory.ucsf.edu/ftd/

Patient Support and Advocacy Resources

- Association for Frontotemporal Degeneration
  http://www.theaftd.org/
- Family Caregiver Alliance: Frontotemporal Dementia
  https://www.caregiver.org/frontotemporal-dementia
- Muscular Dystrophy Association: Facts About Rare Muscular Dystrophies
  https://www.mda.org/sites/default/files/publications/Facts_RareMDs_P-214_0.pdf
- Muscular Dystrophy Canada
  http://www.muscle.ca/
- Muscular Dystrophy UK
  http://www.musculardystrophyuk.org/
- National Organization for Rare Disorders (NORD): Distal Myopathy
  https://rarediseases.org/rare-diseases/distal-myopathy/
- Paget's Association
  http://www.paget.org.uk/

GeneReviews

- Inclusion Body Myopathy with Paget Disease of Bone and/or Frontotemporal Dementia
  https://www.ncbi.nlm.nih.gov/books/NBK1476

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22inclusion+body+myopathy+with+early-onset+Paget+disease+and+frontotemporal+dementia%22+OR+%22Frontotemporal+Dementia%22+OR+%22Paget%27s+Disease+of+Bone%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28inclusion+body+myopathy+AND+paget+disease+AND+frontotemporal+dementia%5BTIAB%5D%29+OR+%28ibmpfd%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- INCLUSION BODY MYOPATHY WITH EARLY-ONSET PAGET DISEASE WITH OR WITHOUT FRONTOTEMPORAL DEMENTIA 1
  http://omim.org/entry/167320

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